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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, RM 1061
Rockville, MD 20852

Re Docket No. 2004N-0133

Part 11, Electronic Record; Electronic Signatures; Public Meeting

The Technical Committee for Electronic Records/Electronic Signatures of PDA Japan is pleased to provide these comments on the FDA Part 11, Electronic Record; Electronic Signatures; Public Meeting. PDA is an international professional association of more than 10,500 individual member scientists having an interest in the fields of pharmaceutical science, manufacturing and quality. PDA Japan is the Japanese Chapter of the PDA and conducts local activities including the Technical Committee for Electronic Records/Electronic Signatures. Our comments were prepared by this committee of experts in the field of Part 11 compliance in Japan. These stakeholders represent major Japanese pharmaceutical companies, engineering companies, software and hardware vendors and consulting companies.

PDA acknowledges and welcomes the re-examination and the new rule making efforts by FDA in the publication of the Federal Register / Vol. 69, No. 68 / Thursday, April 8, 2004 / Notices 18591, "Part 11, Electronic Record; Electronic Signatures; Public Meeting" which issues a request for comments, and we wish to applaud the FDA's progressive and open approach shown in the document.

We are pleased to have the opportunity to provide our comments as input from Japan. We trust that our comments will be received as they were intended; that is, to make the rule making process more global and harmonized.

If you require further information, please feel free to contact me via the information below.

Sincerely,

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Attachment: "Basic and Common Comments", "Comment Grid"

< Basic and Common Comments >

1. **The Role of Rules and Guidances**

We think rules should define high-level requirements, WHAT and WHY clearly, while guidance should show FDA's interpretations and specific examples, HOW. In the Part 11 rule, we do not expect detailed requirements for actual implementation. We think those details are better provided in a series of guidances following re-examination of the rule. Guidances should also be used to provide FDA's current thinking on innovative technologies and how the Part 11 rule should be applied.

We used to disagree among ourselves on Part 11 compliance requirements very much because of ambiguities in the Part 11 rule and related guidances. Those ambiguities made both pharmaceutical industries and vendors in Japan hesitate to move forward with compliance actions. The combination of a clear and simple rule and guidance that provides specific and actual examples will enable our clear understanding and a firm basis for Part 11 compliance activities.

2. **Areas Where We Need Guidance**

We generally recognize a need for "deeper" guidance published by FDA. Guidances need to be published in a timely manner, and they should be updated to eliminate gaps between requirements and ever changing technologies. In some cases, implementation periods may be necessary before enforcement. We believe that by clearly showing how compliance can be achieved in guidance documents or Compliance Policy Guides, this will reduce unnecessary disputes and bring agile compliance actions.

In particularly, a series of Part 11 guidance documents on the following topics is considered necessary.

A. Glossary
B. "Narrow interpretation of scope of part 11 rule" and "Predicate rule records which are required to be Part 11 compliant".
C. Computerized systems validation
D. Risk-based approach
E. System security (including audit trails)
F. Use of new technologies (including remote data entry, bar code, wireless, etc.)
G. Record retention
H. Record copy
I. Electronic signature
J: Hybrid system

In the guidance "Glossary", abstractive terms such as "Authenticity", "Integrity", and regulatory terms of exercising enforcement discretion" should be explained clearly with good examples so that non-English speaking stakeholders may interpret without misunderstanding.

3. **Risk-based Approach**

We agree with the risk-based approach introduced in the Final Guidance for Industry "Part 11, Electronic Records; Electronic Signatures-Scope and Application". However, requirements for too detailed and over-scoped risk assessments are not feasible for actual implementation.

4. **International Harmonization**

We'd like to suggest Part 11 rulemaking activities take into account international harmonization, since rulemaking for electronic records and electronic signatures in the pharmaceutical industry is a global issue. The ICH forum would be a useful platform for discussions.

5. Importance of Involvement of predicate rules experts and alignment activities of predicate rules

Our concern is that the involvement of predicate rule experts in areas of drug application reviews and field inspections has not been adequate during initial rulemaking, revision and enforcement of the Part 11 rule. We think the deep involvement and commitment of predicate rule experts will help ensure the rule makes an important contribution to public health.

We sometimes find inconsistencies and discrepancies among predicate rules. We strongly recommend that the agency build a mechanism to resolve such problems more quickly, make the process more open to industry and establish a process to reflect industry opinions to issue guidances and/or revise the predicate rule.

6. **Time-line for Rule Making**

We hope the FDA will release an expected time-line for the Part 11 re-examination and rulemaking process, which shows important milestones.

< Comment Grid >

Item	Points	Comments
Subpart – A 1.	The agency is interested in comments on FDA's interpretation of the narrow scope of part 11 as discussed in the part 11 guidance and whether part 11 should be revised to implement the narrow interpretation described in the guidance.	The Part 11 rule should be revised to implement the narrow interpretation. However, detailed interpretations of the "narrow scope interpretation" should be included not in the Part 11 rule but in guidance documents.
2.	The agency is interested in comments on whether revisions to definitions in part 11 would help clarify a narrow approach and suggestions for any such revisions.	
3.	The agency is interested in comments on the need for clarification in part 11 regarding which records are required by predicate rules and are therefore required to be part 11 compliant?	Clarification is considered necessary because some predicate rules are not up-to-date and WHAT & HOW requirements are not clear for cases of electronic records and electronic signatures. However, clarification should be provided in the form of guidance. We believe recordkeeping requirements for predicate rules should be defined in predicate rules not Part 11. To try to define them in Part 11 would only lead to further confusion and possible conflicts. Also, the approach to defining recordkeeping requirements in the Part 11 rule should be to define the objectives of the recordkeeping, and not be prescriptive with names and types of records, since technology will change the way records are created and maintained but the purpose for retaining the regulatory records will remain the same.
Subpart – B Overall 1.	The agency is interested in comments on whether there are other areas of part 11 that should incorporate the concept of a risk-based approach, detailed in the part 11 guidance (e.g., those that require operational system and device checks).	The application of any security measures should be based on a sound assessment of the risks involved and the type of system to be deployed. For example, a standalone computer in a locked room would not need the same level of security as a networked computer that has access to the Internet. Once the level of security to be used has been established based on risk, the security measures should be validated for that particular implementation, and the scope and depth of the validation should also be determined based on a risk-assessment of the technology and security measures being implemented. Specifically, the use of device checks and operational checks should also be decided based on a documented risk assessment.
2.	Is additional clarity needed regarding how predicate rule requirements related to subpart B can be fulfilled?	Additional clarity described in guidance documents is always welcome, and in this case needed. However, "how to" information should be provided in guidance documents not rules.
3.	Should the requirements for electronic records submitted	Yes. The requirements for electronic records submitted to FDA should be defined in separate clauses from those of

	to FDA be separate from electronic records maintained to satisfy predicate rule requirements?	electronic records maintained to meet predicate rule requirements. Electronic records in companies may be maintained in various ways and the requirements for them should be less prescriptive and detailed, and allow us to conduct more flexible and practical operations.
4.	Should part 11 continue to differentiate between open systems and closed systems?	Yes. Additional controls are required for open systems, which are different from those for closed systems.
Subpart – B Individual control 1.	Should we retain the validation provision under Sec. 11.10(b) required to ensure that a system meets predicate rule requirements for validation?	Yes, it should be retained. However, additional Part 11 requirements for validation should be clarified in a guidance document. We would like to emphasize the importance of such a document which should provide validation guidance for GxP areas where current predicate rules or guidances do not define clear validation requirements for Part 11 controls. (Note: The Part 11 validation requirement is Sec. 11.10(a) not (b), and it does not seem to reference predicate rule requirements specifically, but is implied by the requirement to ensure "consistent intended performance".)
2.	Are there any related predicate rule requirements that you believe are necessary to preserve the content and meaning of records with respect to record copying and record retention? What requirements would preserve record security and integrity and ensure that records are suitable for inspection, review, and copying by the agency?	It is very limited to preserve security and integrity on records for record copying and record retention with the current networked systems and technologies. Since it is necessary for a company to build assurance system and conduct assurance activities concerning computerized systems., the FDA should show how they intend to monitor and evaluate these systems.
3.	Should audit trail requirements include safeguards designed and implemented to deter, prevent, and document unauthorized record creation, modification, and deletion?	Yes. With the exception of "prevent", this is the main purpose of audit trails, and therefore, they should be designed and implemented to deter and document unauthorized record creation, modification and deletion. However, whether or not to apply audit trails, at which point in the electronic record life-cycle to apply them, and the extent to apply them (e.g. application level, OS level, DB level, etc.) should be based on a documented risk assessment. But if audit trails are used, they should meet the requirements mentioned here, and details about implementation should be given in a guidance document.
4.	In light of how technology has developed since part 11 became effective, should part 11 be modified to incorporate concepts, such as configuration and	No. The terms configuration management and document management are too prescriptive. The Part 11 rule should only define the requirement that changes to software, hardware and associated system documentation be managed and documented in manner which ensure changes do not jeopardize patient safety or product quality. The topic should

	document management, for all of a system's software and hardware?	be included in a guidance document for computerized systems validations.
Subpart – C	Should part 11 address investigations and followup when these security breaches occur?	Yes. There should be some mention in the rule about the basic idea (policy) concerning such investigations, and it is actually touched upon in Sec. 11.300(d), but this is limited to ID code/password related controls. Further details should be explained in a guidance document on system security.
Suppl. Q 1.	What are the economic ramifications of modifying part 11 based on the issues raised in this document?	Where possible, we try to comply and take corrective action if there is clear direction. However, excessive requirements have a large economic impact. Although the change in direction provided by the FDA in last year's guidance where compliance was narrowed was welcome, many companies that had already taken positive steps toward compliance halted or postponed the activities, causing problems. FDA should recognize that in cases where systems are to be upgraded, if the FDA requirements and interpretation are not clear, we will wait and see approach or cancel implementation. From past experience, Part 11 compliance has required huge amounts of resources such as time, personnel, systems and money for developing policies/plans, implementing Part 11 compliant systems or upgrading, and it is difficult to consider that all past efforts have been an effective use of resources, which is a serious issue from the management perspective. In the future, it is hoped that systems can be built with closer cooperation between users, suppliers and FDA in order to develop and build better systems, which will in turn lead to standardized applications and reduced costs.
2.	Is there a need to clarify in part 11 which records are required by predicate rules where those records are not specifically identified in predicate rules? If so, how could this distinction be made?	No. The suggestion above about defining criteria for judging whether an electronic record is within the scope of Part 11 should be used, and any further details (e.g. which particular records) described in guidance documents.
3.	In what ways can part 11 discourage innovation?	Any requirements or description on regulation could give a certain limit for system applicable to each company. It is essential for suppliers to have technology which can both meet functionality of pharmaceutical manufacturing or R&D, and meet Part 11 requirements. It has advantage on improving quality and innovation in the pharmaceutical industry, whereas it is the cause to limit the pharmaceutical industry to introduce advanced technologies.
4.	What potential changes to part 11 would encourage innovation and technical advances consistent with the agency's need to safeguard public health?	Innovation and technology can be promoted by recognizing that not just system technical requirements, but operational aspects also need to be considered, and the system technical requirements reduced as much as possible. The FDA needs to take more positive steps toward providing information, and supporting and evaluating quality assurance and continuous improvement activities. Since hybrid systems will remain predominant for the foreseeable future, the FDA should provide guidance, in consultation with industry, on the requirements for those

		systems as an interim measure. The FDA should recognize that companies would rather not implement applications which have functional limitations that are difficult to use and need special customization, but tend to wait for a mature product with good functionality. Therefore, FDA recognize wider implementation period for efficient mature product, which will be good effect to public health. We would like FDA to understand the situation in other countries also: - The market situation for compliant systems; localized (translated) versions are not released on the local market so quickly. - There are cultural difference in the approach to signatures and signing.
5.	What risk-based approaches would help to ensure that electronic records have the appropriate levels of integrity and authenticity elements and that electronic signatures are legally binding and authentic?	We believe that a risk-based approach which is specific for the Part 11 rule is unnecessary. Generic risk-based approaches to identify, assess, mitigate, monitor and manage risks are applicable and those activities should be conducted. We need an adequate guidance document for practical operations and activities.
6.	What are stakeholder concerns in regards to modifications made to legacy systems in use as of August 1997? Can the use of risk mitigation and appropriate controls eliminate concerns regarding legacy systems?	Systems in use as of August 1997 and enhanced/modified after August 1997 should be treated as legacy systems for which the agency will exercise enforcement discretion. Most legacy systems have functional deficiencies and their upgrading does not compensate for all the deficiencies. The use of operational aspects rather than technical requirements lead to more practical and effective controls on risk mitigation and controls. Part 11 requirements are considered to be necessary when systems are used in high risk environments, regardless of whether they are legacy systems or newly implemented systems. However, the requirements are not easily implemented for legacy systems.
7.	Should part 11 address record conversion?	Yes, it should address conversion. It is necessary for all computerized systems to be able to convert data in some form and addressing this is essential. In this context, issues concerning verification of converted data against original data is more important than that of conversion methodologies or the data conversion process. Specific conversion methodologies should be addressed in guidance documents.
8.	Are there provisions of part 11 that should be augmented, modified, or deleted as a result of new technologies that have become available since part 11 was issued?	Taking into consideration situations where clinical trial data is gathered by systems used by CROs and electronic medical information systems in hospitals, the FDA should clarify its interpretation in guidances as to whether pharmaceutical companies have the responsibility for assuring compliance with Part 11 of systems used by outsourcing companies or third parties.